REMARKS

Claims 110 - 156 are pending.

Claims 115, 118, 119, 125 – 151 are cancelled with entry of this amendment.

Claims 110 – 114, 116 – 117, 120 – 125 and 152 – 156 are under active consideration.

New Claims 157 – 211 are added with entry of this amendment.

Applicants have amended claims 110, 152, and 153 to include a limitation of encapsulating the pancreatic .beta. islet cells. Support for the amendment can be found in the specification at page 4, lines 3 and 4, in Figure 1, and in originally filed claim 19.

Specification

The Examiner has stated that the format of the amendments to the claims does not comply with the Revised Amendment Practice of 37 CFR 1.121, specifically, the text of the withdrawn claims must be identified as "withdrawn" and the text of cancelled claims must be omitted.

Applicants respectfully apologize for the error and submit that the present amendment complies with Revised Amendment Practice of 37 CFR 1.121.

Claim Objections

Claim 110 is objected to due to because the semicolon in line 8 should be deleted. Further, the phrase "exposing the pancreatic islet cells to nicotinamide" in step (ii) should be replaced with "exposing the harvested pancreas to nicotinamide". These errors are corrected by the present amendment.

Claim 117 is objected to due to as being of improper dependent form for failing to further limit the subject matter of a previous claim. This error is corrected by the present amendment.

Claim 120 is objected to because the recitation "at least one of the pancreas" . Applicants

respectfully draw the Examiner's attention to the Applicants' previous Office Action response mailed 2/2/04 at page 3 that shows that claim 120 had been amended to remove the cited recitation at that time. Applicants request clarification from the Examiner.

Claim 123 is objected to due to because it depends from claim 110, and is drawn to further reducing the harvested pancreas mechanically. The Examiner states that since step (iii) of claim 110 has resulted in the isolation of pancreatic islet cells, it does not appear necessary to further reduce the pancreas mechanically or the step of 123 should follow the step (ii) of claim 110. This error is corrected by the present amendment.

Claims 124 and 125 stand objected to due to because the term "quinalone" in the amended claims is not present in general or medical English dictionaries. This typographical error is corrected by the present amendment.

Claim 153 is objected to due to because the phrase "exposing the beta islet cells to nicotinamide" in step (ii) should be replaced with "exposing the harvested pancreas to nicotinamide". These errors are corrected by the present amendment.

Claim 156 is objected to under 37 CFR 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. This error is corrected by the present amendment.

Rejections under 35 USC 112, first paragraph

The Examiner states that claim 117 has been newly rejected under 35 USC 112, first paragraph.

Applicants have amended claim 117 to recite "the compound consists of GPE".

It is respectfully requested that the rejections of claim 117 under 35 USC 112, first paragraph be withdrawn.

The Examiner states that claims 110, 116, and 118 stand rejected under 35 USC 112, first paragraph.

Applicants have cancelled claim 118.

It is respectfully requested that the rejections of claims 110, 116, and 118 under 35 USC 112, first paragraph be withdrawn.

Rejections under 35 USC 112, second paragraph

The Examiner states that claims 110 – 114, 116 – 118, 120 – 125, and 153 – 156 have been newly rejected under 35 USC 112, second paragraph as vague or indefinite. The claims have been amended to address these problems.

Claim 110 has been amended to recite "exposing the harvested pancreas to nicotinamide".
Claim 116 has been amended to recite the limitation "a step".
Claim 118 has been cancelled.
Claim 120 has been amended to recite the limitation "a step".
Claim 153 has been amended to recite "exposing the harvested pancreas to nicotinamide".

It is believed that the above amendments are sufficient to remove the rejections to claims 110 – 114, 116 – 118, 120 – 125, and 153 – 156 under 35 USC 112, second paragraph, and it is respectfully requested that these rejections be withdrawn.

Rejections under 35 USC 102(b)

The Examiner has withdrawn the rejections of claims 110, 111, 113, 115, and 120.

Rejections under 35 USC 102(e)

The Examiner states that Claims 110, 111, 120, and 123 stand rejected under 102(e) as anticipated by Elliott (US Patent Nos. 6,146,653 and 6,090,400).

Applicants herewith attach a declaration under 37 CFR 1.132 signed by one of the inventors, Robert Bartlet Elliott, stating that the claimed invention was not described in a patent granted on an application for patent by another filed in the United States before the invention by the applicant. In addition, Applicants have amended claim 110 to include a limitation of

encapsulating the porcine islet cells. It is respectfully requested that the rejection of Claims 110, 111, 120, and 123 under 35 USC 102(e) be withdrawn.

Rejections under 35 USC 102(f)

The Examiner states that Claims 110, 111, 120, and 123 stand rejected under 102(f). The Examiner asserts that the applicants did not invent the subject matter now claimed.

Applicants herewith attach a declaration under 37 CFR 1.132 signed by one of the inventors, Robert Bartlet Elliott, stating that the one inventor of the claimed invention was simultaneously the same inventor on granted patents USPN 6,146,653 or 6,090,400. In addition, Applicants have amended claim 110 to include a limitation of encapsulating the porcine islet cells. It is respectfully requested that the rejection of Claims 110, 111, 120, and 123 under 35 USC 102(f) be withdrawn.

Rejections under 35 USC 103(a)

The Examiner has rejected Claims 110, 111, 113, 120, and 152 – 156 under 35 USC 103(a) as being obvious over Rayat et al. in view of Nielsen et al., and as evidenced by Kallmann et al. and Elliott et al.

Applicants have amended claims 110, 152, and 153 to include a limitation of encapsulating the porcine islet cells. The limitation of encapsulating the porcine islet cells would not be subject to the current rejections for the following reasons. Rayat et al. and Nielsen et al. do not teach or suggest encapsulating porcine islet cells that have been treated with nicotinamide. Neither do any of the cited references, alone or in combination, teach or suggest encapsulating porcine islet cells treated with nicotinamide. For an invention to be obvious, every element of the claimed invention must be found in the combined references (In re Vaeck, 947 F.2d 488; 20 USPQ2d 1438 (Fed. Cir. 1991)), and this is not the case here. It would not, therefore, have been obvious, in view of the cited references, to practice the invention as presently claimed. It is respectfully requested that the rejection of Claims 110, 111, 113, 120, and 152 – 156 under 35 USC 103(a) be withdrawn.

The Examiner has rejected Claim 112 under 35 USC 103(a) as being unpatentable over Rayat et al., and Nielsen et al., as applied to claims 110, 111, 113, 120, and 152-156 above, and further in view of Brandhorst et al.

Applicants have amended claims 110, 152, and 153 to include a limitation of encapsulating the porcine islet cells. The limitation of encapsulating the porcine islet cells would not be subject to the current rejections for the following reasons. Rayat et al. and Brandhorst et al. do not teach or suggest encapsulating the porcine islet cells that have been treated with liberase. Neither do any of the cited references, alone or in combination, teach or suggest encapsulating porcine islet cells treated with liberase. For an invention to be obvious, every element of the claimed invention must be found in the combined references (In re Vaeck, 947 F.2d 488; 20 USPQ2d 1438 (Fed. Cir. 1991)), and this is not the case here. It would not, therefore, have been obvious, in view of the cited references, to practice the invention as presently claimed. It is respectfully requested that the rejection of Claim 112 under 35 USC 103(a) be withdrawn.

The Examiner has rejected Claim 114, 116, and 123 under 35 USC 103(a) as being unpatentable over Rayat et al., and Nielsen et al., as applied to claims 110, 111, 113, 120, and 152-156 above, and further in view of Clark et al. and Maysinger et al.

Applicants have amended claim 110 to include a limitation of encapsulating the porcine islet cells. The limitation of encapsulating the porcine islet cells would not be subject to the current rejections for the following reasons. Rayat et al., Clark et al, and Maysinger et al. do not teach or suggest encapsulating porcine islet cells cultured in a defined medium comprising IGF-1 and HSA. Neither do any of the cited references, alone or in combination, teach or suggest encapsulating the porcine islet cells. Furthermore, Maysinger et al. do not teach or suggest using a trauma preventing agent as suggested by the Examiner. In fact, Maysinger et al. suggest that the decrease in .beta. cell mass following transplantation may be an effect of apoptosis *in vivo*. For an invention to be obvious, every element of the claimed invention must be found in the combined references (In re Vaeck, 947 F.2d 488; 20 USPQ2d 1438 (Fed. Cir. 1991)), and this is

not the case here. It would not, therefore, have been obvious, in view of the cited references, to practice the invention as presently claimed. It is respectfully requested that the rejection of Claims 114, 116, and 123 under 35 USC 103(a) be withdrawn.

The Examiner has rejected Claim s 116 and 117 under 35 USC 103(a) as being unpatentable over Rayat et al., and Nielsen et al., Clark et al. and Maysinger et al. as applied to claims 110, 113, 114, 116, 120, 123, and 152-156 above, and further in view of Saura et al.

Applicants have amended claim 110 to include a limitation of encapsulating the porcine islet cells. The limitation of encapsulating the porcine islet cells would not be subject to the current rejections for the following reasons. Rayat et al. and Saura et al. do not teach or suggest encapsulating porcine islet cells that have been treated with GPE. Neither do any of the cited references, alone or in combination, teach or suggest encapsulating the porcine islet cells. For an invention to be obvious, every element of the claimed invention must be found in the combined references (In re Vaeck, 947 F.2d 488; 20 USPQ2d 1438 (Fed. Cir. 1991)), and this is not the case here. It would not, therefore, have been obvious, in view of the cited references, to practice the invention as presently claimed.

Applicants respectfully draw the Examiner's attention to the specification at page 20,lines 26-27, where they disclose that "(t)he results suggest that GPE could be used during porcine cell islet cell culture to improve (emphasis added) the quality and function of the cells before transplantation". The prior art, such as Suara et al., generally attribute the effect of GPE as having a role in blocking apoptosis after injury and in disease. In view of these unexpected and beneficial results, as well as the arguments and amendments discussed above, it is respectfully requested that the rejection of Claims 116 and 117 under 35 USC 103(a) be withdrawn.

The Examiner has rejected Claim s 121 and 122 under 35 USC 103(a) as being unpatentable over Rayat et al., and Nielsen et al., Clark et al. as applied to claims 110, 111, 113, 120, and 152-156 above, and further in view of Pu et al.

Applicants have amended claim 110 to include a limitation of encapsulating the porcine

islet cells. The limitation of encapsulating the porcine islet cells would not be subject to the current rejections for the following reasons. Rayat et al. and Pu et al. do not teach or suggest encapsulating porcine islet cells that have been treated with lignocaine. Neither do any of the cited references, alone or in combination, teach or suggest encapsulating the porcine islet cells. For an invention to be obvious, every element of the claimed invention must be found in the combined references (In re Vaeck, 947 F.2d 488; 20 USPQ2d 1438 (Fed. Cir. 1991)), and this is not the case here. It would not, therefore, have been obvious, in view of the cited references, to practice the invention as presently claimed.

Applicants respectfully draw the Examiner's attention to the specification at page 13, lines 17-18 and at page 20, line 32 and page 21, lines 1- 19 where Applicants describe the culture conditions used to provide a xenotransplantable porcine islet that include lignocaine. It is well known in the art that lignocaine is a species of the phospholipase A_2 inhibitor anaesthetics.

Of note, Applicants found that culturing the pig islets with lignocaine unexpectedly increased the viability of the pig islets by six-fold as measured using the comparative insulin release from the islets when compared with culturing without (see page 21, lines 18-19). One of skill in the art would not have had a reasonable expectation that any anesthetic would affect insulin secretion from porcine islets. In view of these unexpected and beneficial results, as well as the arguments and amendments discussed above, it is respectfully requested that the rejection of Claims 121 and 122 under 35 USC 103(a) be withdrawn.

The Examiner has rejected Claim s 124 and 125 under 35 USC 103(a) as being unpatentable over Rayat et al., and Nielsen et al., Clark et al. as applied to claims 110, 111, 113, 120, and 152-156 above, and further in view of Boss et al. and Champion et al.

Applicants have amended claim 110 to include a limitation of encapsulating the porcine islet cells. The limitation of encapsulating the porcine islet cells would not be subject to the current rejections for the following reasons. Rayat et al. Champion et al., and Boss et al. do not teach or suggest encapsulating porcine islet cells that have been treated with quinolone antibiotics such as ciproflaxin (ciproxin). Neither do any of the cited references, alone or in combination,

teach or suggest encapsulating the porcine islet cells. For an invention to be obvious, every element of the claimed invention must be found in the combined references (In re Vaeck, 947 F.2d 488; 20 USPQ2d 1438 (Fed. Cir. 1991)), and this is not the case here. It would not, therefore, have been obvious, in view of the cited references, to practice the invention as presently claimed.

Applicants respectfully draw the Examiner's attention to the specification at page 12, lines 9-11 where Applicants describe the culture conditions used to provide a xenotransplantable porcine islet that include the antibiotic CIPROXIN. Applicants and the Examiner have noted in previous correspondence that CIPROXIN is a species of the quinolone antibiotics. It is well known in the art that CIPROXIN is the trade name for ciprofloxacin species of the quinolone antibiotics.

Applicants found that culturing the pig islets with CIPROXIN unexpectedly increased the viability of the pig islets as measured using the comparative insulin release from the islets when compared with culturing with antibiotics having a different antibiotic mechanism , such as penicillin and streptomycin (see page 21, lines 29-30 and Figure 4). One of skill in the art would not have had a reasonable expectation that any antibiotic would affect insulin secretion from porcine islets and the results disclosed in the specification show that penicillin and streptomycin do not affect insulin secretion from porcine islets, the effect being no different from untreated control islets (see Figure 4).

In view of these unexpected and beneficial results, as well as the arguments and amendments discussed above, it is respectfully requested that the rejection of Claims 124 and 125 under 35 USC 103(a) be withdrawn.

Non-Statutory Obviousness-Type Double Patenting Rejection

The Examiner has stated that Claims 110, 111, 120, and 123 stand rejected under the judicially created doctrine of obvious double patenting as being unpatentable over claims 11, 13, and 14 of US Patent No. 6,146, 653

Applicants have amended claim 110 to include a limitation of encapsulating the porcine islet cells and which would not be subject to the current rejections.

The claims as presently amended are significantly distinct from those of Patent No. 6,146, 653, and any such claims that would issue would not be co-extensive in scope with those of the previously issued patent. In view of this, the present non-statutory double patenting rejection would not be rightly applicable, and it is respectfully requested that the rejection of Claims 110, 111, 120, and 123 be withdrawn.

New Claims

Applicants have submitted new claims for consideration and entry by the Examiner. In considering new claims 167, 168, 179 – 181, 192, 205, and 206, Applicants respectfully draw the Examiner's attention to the specification at page 12, lines 9-11 where Applicants describe the culture conditions used to provide a xenotransplantable porcine islet that include the antibiotic CIPROXIN. Applicants and the Examiner have noted in previous correspondence that CIPROXIN is a species of the quinolone antibiotics. It is well known in the art that CIPROXIN is the trade name for ciprofloxacin species of the quinolone antibiotics.

The present disclosure describes data that shows that culturing the pig islets with CIPROXIN unexpectedly increased the comparative insulin release from the islets when compared with culturing with antibiotics having a different antibiotic mechanism , such as penicillin and streptomycin (see page 21, lines 29-30 and Figure 4). One of skill in the art would not have had a reasonable expectation that any antibiotic would affect insulin secretion from porcine islets and the results disclosed in the specification show that penicillin and streptomycin do not affect insulin secretion from porcine islets, the effect being no different from untreated control islets (see Figure 4).

In considering new claims 161 – 164, 174 – 176, 186 – 189, 194, and 199 – 201, Applicants respectfully draw the Examiner's attention to the specification at page 13, lines 17-18 and at page 20, line 32 and page 21, lines 1- 19 where Applicants describe the culture conditions used to provide a xenotransplantable porcine islet that include lignocaine. It is well known in the art that lignocaine is a species of the phospholipase A_2 inhibitor anaesthetics.

Applicants found that culturing the pig islets with lignocaine unexpectedly increased the viability of the pig islets by six-fold as measured using the comparative insulin release from the islets when compared with culturing without (see page 21, lines 18-19). One of skill in the art would not have had a reasonable expectation that any anesthetic would affect insulin secretion from porcine islets.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is in a condition for allowance, and request that the Examiner withdraw the outstanding rejections.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Attorney. Should anything further be required, a telephone call to the undersigned, at (510) 537-2040, is respectfully invited.

Respectfully submitted,

FACTOR & LAKE

Dated: November 20th 2004

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One of Attorneys for Applicant

Certificate of Faxing

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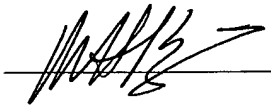
On: 20th November, 2004 By:  Printed: Matthew Kaser